Observation of At-211 accumulated cells using a real-time alpha-particle imaging system

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Technology to Visualize the spatial distribution of high-resolution alpha particles has emerged as crucial for assessing their dispersion in cellular and animal models, facilitating the advancement of novel radiopharmaceuticals and targeted alpha-particle therapy. Radioluminescence microscopy (RLM) is an advanced in vitro radionuclide imaging technique designed for the high-resolution visualization of charged particles. This method enables real-time imaging of charged particles within a 1 mm^2 field of view. RLM comprises a high-sensitivity camera integrated with a microscope objective lens, capturing emissions from a thin scintillator positioned above or below a radiopharmaceutical-containing sample. Alpha-particle imaging detectors employing this methodology have been documented in previous studies.[1,2] Our research group has also been actively developing real-time alpha-particle imaging detectors based on this approach and has successfully achieved imaging of alpha particles emitted from Am-241 with a spatial resolution of 0.48 μm.[3,4]

In this study, we designed and developed a high-resolution, real-time alpha-particle imaging detector to visualize the distribution of alpha particles emitted from At-211 internalized by cells and quantify radioactivity by leveraging findings from our previous research. Figure 1 presents a conceptual schematic of the developed detector. In this system, a 100 μm-thick GAGG:Ce scintillator single-crystal plate is positioned atop the cultured cells within a cell culture dish, analogous to a glass slide. An objective lens, focused on the GAGG:Ce scintillator, is mounted above the scintillator plate to magnify the emitted scintillation light, which is subsequently captured by a cooled CMOS sensor via an imaging lens. In this experiment, mesenchymal stem cells transduced with or without Na-Iodide Symporter (NIS) were cultivated on chamber slide at a concentration of 3.6×10^4 cells per well. NIS works as a halogen family transporter, and contributes At-211 uptake. Subsequently, 500 kBq of NaAt was administrated to each chamber and waited for At-211 internalization by the cells. After 30 min incubation, chamber slides were washed by pure water, fixed by formalin, and applied to alpha particle specialized imaging.

The optical image of the cells was acquired through a GAGG:Ce scintillator single-crystal plate (Fig. 2(a)).

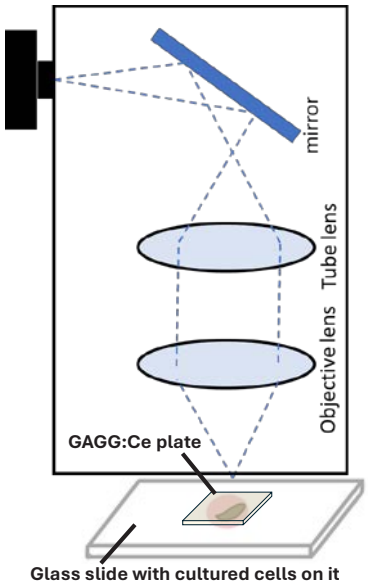

Fig. 1. Conceptual schematic of the developed detector.

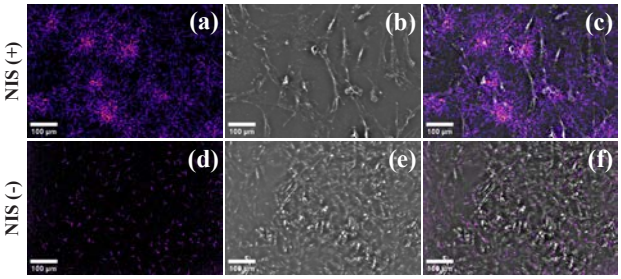

Fig. 2. Acquired images using the developed detector: The upper panels present images of the cells with NIS transduction [shown as NIS (+)]. The lower panels are figures of the cells without NIS transduction [shown as NIS (−)]. (a&d) Images of alpha particles emitted by At-211 internalized by the cells, (b&e) optical images of cultured cells, (c) merged images of (a) and (b), (f) merged images of (d) and (e).

At this stage, the objective lens was precisely focused on the cells. Owing to the transparency of the GAGG:Ce scintillator, a high-clarity optical image of the cells was obtained. Subsequently, the objective lens was refocused a few micrometers inward from the surface of the GAGG:Ce scintillator to conduct an imaging test for alpha particles emitted by At-211 within the cells. The results are presented in Fig. 2(b). For alpha-particle imaging, 600 one-second exposures were

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acquired and subsequently processed by stacking and projecting along the Z-axis. Fig. 2(c) presents a composite image integrating Fig. 2(a) and 2(b). As shown in Fig. 2(c), the distribution of alpha particles emitted from At-211 was successfully superimposed onto the cellular image, enabling their simultaneous visualization within a single frame.

In this study, we designed and developed an imaging detector capable of direct and real-time imaging or the alpha particles emitted from At-211 internalized by cells. Consequently, we successfully visualized the distribution of alpha particles released from At-211 within cells transported by NIS on an event-by-event basis. A key challenge for future research is to establish a methodology for quantifying radioactivity from the acquired images. The findings of this study hold significant importance for evaluating the efficiency of At-211 uptake into cells, thereby contributing to the development of At-211-based therapeutic agents in the future.

References

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